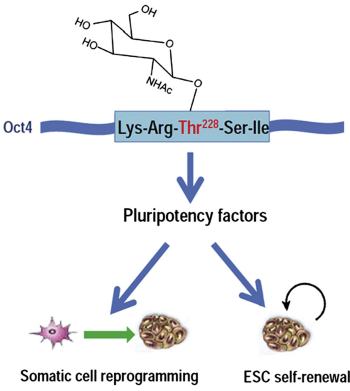
Cell Stem Cell

In This Issue



New Neural Tricks for an Old Diabetes Drug

WANG ET AL., PAGE 23

The diabetes drug metformin activates the aPKC-CBP pathway to promote neurogenesis, thereby improving spatial learning. By targeting neural stem cells to enhance neural function, metformin provides a candidate pharmacological approach for nervous system therapy. In Translation by Potts and Lim.

Damage Control Leads to Bone Marrow Failure in FA

CECCALDI ET AL., PAGE 36

Progressive bone marrow failure in Fanconi anemia patients stems from an exacerbated p53/p21 stress response and DNA damage, which leads to hematopoietic stem and progenitor cell loss that starts during fetal development. In Translation by Dumitriu and Young.

Osteogenic MSCs Need Histone Demethylation to Commit

YE ET AL., PAGE 50

Mesenchymal stem cells (MSCs) increase their levels of H3K9me3 and H3K27me3 chromatin marks in a model of osteoporosis. In human MSCs, their removal by KDM4B and KDM6B demethylases is required for osteogenic lineage commitment.

Pluripotency Never Tasted So Sweet

JANG ET AL., PAGE 62

Oct4 and Sox2 are modified by *O*-GlcNAc in ESCs, which is important for Oct4-mediated transcription of many pluripotency genes. Blocking *O*-GlcNAc disrupts ESC self-renewal and reprogramming to iPSCs. (Top image.)

An eXISTential Crisis: When Female hiPSCs Lose Their Somatic Xi

ANGUERA ET AL., PAGE 75 AND TOMODA ET AL., PAGE 91

Epigenetic variability in hiPSCs may impact their potential for future application. Anguera et al. show that XIST loss in female hiPSCs correlates with oncogene upregulation, a faster growth rate, and poor cell differentiation. Tomoda et al. show that growth conditions, particularly the presence of SNL feeder cells and LIF, strongly influence the degree of X-reactivation seen in female hiPSCs. Minireview by Anton Wutz.

Single-Factor Direct Reprogramming to iNSCs

RING ET AL., PAGE 100

Under specific growth conditions, mouse fibroblasts can be reprogrammed with a single factor, Sox2, to form induced neural stem cells (iNSCs) that self-renew, have trilineage differentiation potential, and integrate after transplantation into the brain. A similar approach seems to work for human fibroblasts.

Pluripotency Proceeds without a Blimp1

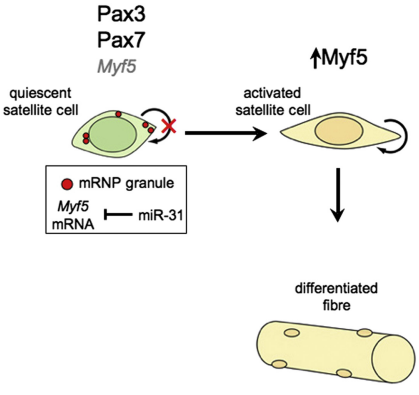
BAO ET AL., PAGE 110

Blimp1, which is required for primordial germ cell (PGC) fate, is dispensable for the derivation of ESCs and EpiSCs and for reprogramming. This suggests that acquisition of pluripotency does not entail an obligatory route through a Blimp1-positive PGC-like state. Preview by Amander Clarke.

Sequestering Strength in RNP granules

CRIST ET AL., PAGE 118

Quiescent muscle satellite cells transcribe the myogenic determination gene *Myf5*, but prevent activation of the myogenic program by sequestering *Myf5* mRNA in mRNP granules. After satellite cell activation, the mRNP granules dissociate and Myf5 protein accumulates, leading to differentiation. (Bottom image.)



Less *GrHl3* Is More for Epidermal Progenitor Self-Renewal

MISTRY ET AL., PAGE 127

Maintenance of human epidermal progenitor cells requires exosome function, and more specifically degradation of *GRHL3* transcripts, to promote self-renewal and prevent premature differentiation.